REMARKS

Applicants request entry of the amendments to the claims and specification. The amendments introduce no new matter. Provision for 3-months extension of time accompanies this paper.

37 CFR § 1.75(c) Claim Objection

Claims 56-59, 61, 63-65 and 67-69 have been amended by presenting a new set of claims 70-74 which are directed to the same elected invention and narrower in scope. The claim objection is therefore made moot.

Disclosure Objection

The office objected to references to Figures in the Specification of the instant application, which were not explicitly shown. These Figures are explicitly shown in application serial no. 60/157,275 (filing date September 30, 1999), which is a provisional patent application, incorporated by reference into the specification of the instant application at the time this application was filed. Therefore, addition by amendment of the information contained within these Figures into the instant application does not constitute new matter.

Paragraphs containing the objected disclosure have been deleted by amendment and replaced.

35 USC § 112, first paragraph Rejection

The Office rejected claims 56-59, 61, 63-65 and 67-69 under 35 USC § 112, first paragraph as allegedly not enabled. The rejection was based upon the nature of the invention ("..administration of a large number of steroid derivatives"), the predictability or lack thereof in the art ("…Chang, et al. show that there is great unpredictability in activities in various derivatives in dehydroepiandrosterone"), the presence or absence of working examples ("single working example…wherein one or (sic) R5 or R6 is carbonate…"), the breadth on the claims ("[t]he claims encompass a very large number of species."….[t]he specification discloses a single species of a compound wherein

R5 or R6 is a carbonate…" 'in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims'…") and the quantity of the experimentation needed ("Chang et al…disclose that among 22 derivatives/metabolites of dehydroepiandrosterone, only 4 steroids were found that have no androgenic activity and could block the Adiol-induced AR transactivation…[b]ecause there is no way to predict a priori which compounds would be active from the specification or chemical structures alone, and extraordinary amount of trial and error experimentation is required…").

Firstly, Applicants object to citation of the Chang, et al. reference in its formulation of this rejection. The Chang, et al. reference had been previously considered by the Office as evidenced by Examiner's initials dated February 01, 2002 alongside the reference, which Applicant had provided in an IDS, received by the technical center on January 25, 2001. Therefore, citation of the Chang, et al. reference at this stage of prosecution represents piecemeal examination, since the Office should have made its 35 USC § 112, first paragraph rejection based upon its first office action on the merits mailed February 05, 2005. In particular, 37 CRF 1.104 (b) states, in part, "The examiner's action will be complete as to all matters, except that in appropriate circumstances…". Furthermore, MPEP 707.07(g) provides that "Piecemeal examination should be avoided as much as possible. The examiner ordinarily should reject each claim on all valid grounds available..." Such piecemeal examination presents a financial hardship for the assignee, since delays for demonstrating patentability to investors are being incurred. Therefore, with a new ground of rejection made by the Office, which should have been made in a previous office action, Applicant's respectfully request the next action on the merits be made non-final.

Secondly, Applicants respectfully traverse these statements the Office has made in formulating this rejection. Of the eight Wands factors for assessing

enablement under 112 first paragraph, the Office has not provided support for three of these factors namely, the state of the prior art, the relative skill of those in the art and the amount of direction or guidance presented. In re Wands, 858 F.2d 731, 735 (Fed. Cir. 1988). The Applicants discuss these factors as follows and will then address other factors relied upon by the Office.

The relative skill of those in the art

The ordinary practitioner in the art to which the invention most closely pertains will have a PhD degree and experience in drug discovery and development and will have a strong appreciation for structure-activity relationships. Thus, the skill level for this practitioner will be high. Furthermore, to select compounds from Applicants' genera for the purpose of practicing Applicant's invention, significant guidance to this practitioner is provided in Applicants' disclosure. This guidance is in the form of cell-based assays measuring androstene receptor (AR) transcriptional activity, the nature of which was routine at the time of Applicants' filing. In the instant application, Applicants describe a two-tier assay which first measures AR transcriptional activity in an AR negative PC-3, a prostate cancer cell line. Compounds with very little androgenic activity at 1 μM in this setting are then screened for their ability to inhibit AR transcriptional activity mediated by androstene (Adiol). These specific assays were known in the art prior to Applicants' filing as evidenced in Chang, et al. (of record) and in Miyamoto, H. et al. (*Proc. Natl. Acad. Sci USA*, 95:11083-11088, 1998, of record). However, it should be noted that Applicants' invention is the discovery of dehydroepiandrosterone (DHEA) analogs that inhibit the AR transcriptional activity of Adiol, which will be a point expanded upon in a subsequent section.

The state of the prior art

The use of in vitro screens for understanding the binding mode of steroids to their receptors for the purpose of developing structure activity relationships

has been an area of interest for a number of years. This is evidenced by publications by Waller, et al. ("Three-dimensional quantitative structure-activity relationships for androgen receptor ligands" *Toxicol. Appl. Pharmacol.* 137:219-227, 1996, newly cited) and Loughney, et al. ("A comparison of progestin and androgen receptor binding using the CoMFA technique", *J. Comp. Aided Drug Design* 6:567-581, 1992, newly cited). Therefore, the state of the art at the time of Applicants' disclosure was (and remains) high.

The quantity of experimentation necessary

In response to the Office's argument with regards to the quantity of experimentation needed, the CAFC has "…held that a patent specification complies with the statute even if a `reasonable' amount of routine experimentation is required in order to practice a claimed invention, but that such experimentation must not be `undue.' See, e.g., Wands, 858 F.2d at 736-37, 8 USPQ2d at 1404 (`Enablement is not precluded by the necessity for some experimentation ... . However, experimentation needed to practice the invention must not be undue experimentation. The key word is ``undue," not ``experimentation.") (footnotes, citations, and internal quotation marks omitted). In re Wands, we set forth a number of factors which a court may consider in determining whether a disclosure would require undue experimentation." Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 52 USPQ2d 1129 (Fed. Cir. 1999) and ``[t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." United States v. Telectronics, Inc. 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988), cert. denied, 490 U.S. 1046 (1989) citing Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). The courts have also held that ``Enablement is not precluded by the necessity for some experimentation such as routine screening". In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). And

the USPTO has also stated "`[R]outine experimentation' may involve rather extensive studies without straying from `undue' experimentation. ..." in a case were there was a high level of skill in this art at the time the application was filed and all the methods needed to practice the invention were well-known. Ex parte D, 27 USPQ2d 1067, 1069-70 (Bd. Pat. App. & Int'f 1993). Furthermore the USPTO has also stated on several occasions that '… a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed. "Ex parte Jackson, 217 USPQ 804, 807 (Bd. Pat. App. & Int'f 1982) and Ex parte Forman 230 USPQ 546, 547-548 (Bd. Pat. App. & Int'f 1986).

The amount of direction or guidance presented

In the prior art (Cheng, et al.; Miyamoto, et al.) and in Applicants' disclosure, routine screens for enablement are provided, which is highlighted by the statement in Chang, et al. on page 11177 beginning on line 6 stating "We have developed a reliable method to screen compounds that can block the Adiol-induced AR transactivation…." Given the relative skill of those in the art described previously and the routine nature of the screening assays, which is available from the prior art and Applicants' disclosure, Applicants assert that more than sufficient guidance has been given and therefore the degree of experimentation that may be involved does not require "…ingenuity beyond that to be expected of one of ordinary skill in the art" (in Fields v. Conover (1971), 443 F.2d at 1390-91, 170 USPQ at 279) and allows the practitioner to practice the invention "…without resort to independent invention…" (in Franc-Strohmenger & Cowan, Inc. v. Arthur Siegman, Inc. 27 F.2d 785 (2d Cir. 1928)), which are thresholds for undue experimentation that have been enunciated by the courts.

The presence or absence of working examples

As to the number of working examples required, the following quotations indicate the enablement inquiry must be based upon the disclosure as a whole and that even in complex technologies, even the complete absence of working example is not fatal.

(1) "… not to say that the specification itself must necessarily describe how to make and use every possible variant of the claimed invention, for the artisan's knowledge of the prior art and routine experimentation can often fill gaps…" Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993).

(2) "We recognize that working examples are desirable in complex technologies…" "…[n]evertheless, as acknowledged by the board, examples are not required to satisfy section 112, first paragraph (internal citations omitted)". In re Strahilevitz, 668 F.2d 1229, 212 USPQ 561 (CCPA 1982).

(3) "…it is the nature of the disclosure rather than the number of the examples given which determines the sufficiency of the disclosure to support..the claim.". In re Cavallito, 282 F.2d 363, 127 USPQ 206 (CCPA 1960).

(4)"…the is no magical relation between the number of representative examples and the breath of the claims; the number and variety of examples are irrelevant if the disclosure is 'enabling'…" In re Barr, 444 F.2d 588; 170 USPQ 330 (CCPA 1971) citing In re Borkowski, 422 F.2d 904, 910, 164 USPQ 642, 646 (1970).

The predictability or unpredictability of the art

The Office's characterization of the results presented in Chang, et al. that only 4 DHEA analogs of 22 compounds tested were found to have little AR transcriptional activity and could block the Adiol-induced AR transactivation as evidence for unpredictability in the art ("…Chang, et al. show that there is great unpredictability in activities in various derivatives of dehydroepiandrosterone"), misapprehends the gist of the invention disclosed in the instant application. The invention relates to the discovery of DHEA analogs that are able to inhibit the AR

transcriptional activity peculiar to Adiol. The method of discovery for such compounds involved screening of DHEA analogs which are essentially devoid of AR transcriptional activity in a AR-negative prostate cancer cell line (AR-negative PC-3) that still exhibits Adiol induced AR transcriptional activity against AR-positive PC-3 cells to determine if such compounds would inhibit AR-transcriptional activity in the presence of Adiol. With the universe of DHEA analogs reduced to those devoid of "classic" AR transcriptional activity, 4 out of 10 compounds were found to inhibit AR-transcriptional activity in an AR-positive prostate cancer. By expanding the reference point to the initial screen of 22 DHEA analogs for those compounds devoid of "classic" androgenic activity, from which the Applicant's selected for further study, the Office has magnified the factor of unpredictability and has essentially held the manner in which the invention was discovered against the Applicant. So doing is prohibited. "Patenentability shall not be negatived by the manner in which the invention was made." (35 USC § 103). "patent acquisition does not require any threshold level of effort or ingenuity; 35 U.S.C. § 103 Revision Notes and Legislative Reports, 1952 Notes. The courts have expanded on this by stating "the path that leads an inventor to the invention is expressly made irrelevant to patentability by statute". *CFMT, Inc. and CFM Technologies, Inc., v. Yieldup International Corp.*, 349 F.3d 1333 (Fed. Cir. 2003) *citing Life Techs., Inc. v. Clontech Labs., Inc.*, 224 F.3d 1320, 1325 (Fed. Cir. 2000).

The breath of the claims

"The sufficiency of a disclosure depends not on the number but rather on the nature of the claimed compounds per se and the nature of the supporting disclosures. If a claim covers compounds that are closely related, a comparatively limited disclosure may be sufficient to support it." In re Cavallito, 282 F.2d 363, 127 USPQ 206 (CCPA 1960). Applicants have amended their claims to retain the close relationship between compounds covered therein and have not made these amendments in response to any rejection, and therefore

Applicants reserve the right to claim additional compounds no longer claimed in subsequent continuing applications.

In conclusion, Applicant's assert the Office has not meet its burden to show that a person of ordinary skill in the art, following the teachings of the specifications, would not be able to practice the claimed invention. (" a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support". In re Marzocchi 439 F.2d 220, 223 (CCPA 1971); (1971)).

35 USC § 102(e) Rejection

Applicants with this response submit an Affidavit under 37 CRF § 1.131, which includes exhibits to support the assertions made, showing they alone were the inventors of the subject matter present in Chang, et. al, which forms the basis for the 102(e) rejection. The affidavit declares that Henry A. Lardy and Padma Marwah, the inventors of the instant application and co-authors of the Chang, et al reference, together or individually, selected compounds for testing in the assays described in the reference based on structure-activity relationships, prepared compound 10 (androst-5-ene-3β-methylcarbonate-7,17-dione) and shipped this and all other compounds to the Chang laboratory where the assay were conducted blinded, providing only the molecular weight and furthermore, only the inventors of the instant applicant knew the results and chemical structures for individual compounds in the assay before any personnel in Dr. Chang's laboratory was aware of this. In view of the facts, none of the subject matter that is now disclosed or claimed in the instant patent application and disclosed in Chang, et al. was or could have been invented by or derived from

any of the other Chang, et al. authors. Furthermore, Henry A. Lardy, contributed the Chang et al. reference for publication as shown at the attribution statement: "*Contributed by Henry Lardy, August 5, 1999*" on page 11173. The information in this publication was therefore necessarily in the possession of the inventors of the instant applicant before the article published and the manuscript that the journal received for publication on August 5, 1999 was thus a written reduction to practice for all of the information in the article that existed on that date, which predates the article's publication on September 28, 1999.

Since the inventors of the subject matter in the instant application are the same inventors of the subject matter in Chang, et al. and were under a duty to assign to a common assignee at the time the invention was made, the 102(e) is made moot.

Conclusion

Applicants believe that all of the issues the Office raised in the office action mailed on August 22, 2006 are now obviated and that the claims are in condition for allowance.

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